We claim:.

- 1. A non-radioactive hybridization as ay for the detection of a target nucleic acid sequence in a biological sample the improvement comprising the steps of:
 - a) hydrolyzing the sample with a base;
- b) hybridizing a nucleic acid sequence in the treated sample to a complementary nucleic acid probe to form a houble-stranded hybrid;
- c) capturing the hybrid onto a solid phase to which an antihybrid antibody or anti-hybrid fragment has been immobilized; and,
 - d) eliminating any non-hybridized probe; and
 - e) detecting the bound hybrid.
- 2. The assay of claim 1 wherein the non-hybridized probe is eliminated by digestion with an enzyme.
- 3. The assay of claim 1 wherein the target nucleic acid is DNA selected from the group consisting of, human papillomavirus DNA, hepatitis B DNA, and *Chlamydia* DNA.
- 4. The assay of claim wherein the probe is an RNA sequence complementary to target DNA.
- 5. The assay of claim 1 wherein the double-stranded hybrid is an RNA/DNA hybrid.
- 6. The assay of chaim 1 wherein the digesting enzyme is RNAase.
- 7. The assay of claim 1 wherein the concentration of probe is between 1 and 500 ng/ml.
- 8. The assay of claim.1 wherein the concentration of probe is between 20 and 200 ng/ml.
- 9. The assay of claim 1 wherein the concentration of probe is approximately 75 ng/ml.
- 10. The assay of claim 1 wherein the base is sodium hydroxide in a concentration of between 0.1 and 2.0 M, incubated with the sample at a temperature between 20 and 100°C for a period of between 5 and 120 minutes.

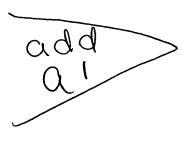
- 11. The assay of <u>claim</u> 1 wherein the base is sodium hydroxide in a concentration of between 0.2 and 0.8 M, incubated with the sample at a temperature between 60 and 70°C for a period of between 30 and 60 minutes.
- 12. The assay of claim 1 wherein the base is sodium hydroxide in a concentration of approximately 0.415 M, incubated with the sample at a temperature of approximately 65°C for a period of approximately 45 minutes.
- 13. The assay of claim 6 wherein the RNAase is added to the sample in a concentration between 0.01 and 1 mg/ml and incubated with the sample at a temperature between 4 and 45°C for a period of between 5 minutes and 24 hours.
- 14. The assay of claim 6 wherein the RNAase is added to the sample in a concentration between 0.05 and 0.5 mg/ml and incubated with the sample at a temperature between 20 and 30°C for a period of between 10 and 60 minutes.
- 15. The assay of claim 6 wherein the RNAase is added to the sample in a concentration of approximately 0.2 mg/ml and incubated with the sample at room temperature for a period of approximately 30 minutes.
- 16. The assay of <u>claim</u> 1 further comprising diluting the probe in a buffer that restores the sample to a neutral pH.
- 17. The assay of claim 16 wherein the buffer comprises 2-[bis(2-Hydroxyethyl) amino] ethane sulfonic acid and sodium acetate.
- 18. A kit for the detection of a target nucleic acid sequence for diagnosing genetic defects, microbial or viral infections in a biological sample comprising:

a) a sample transport medium for stabilization of the biological sample;

b) a base for treating the sample by nicking and degrading the target nucleic acid sequence therein;

/ c) a probe complementary to the treated target nucleic acid sequence for formation of a double-stranded nucleic acid hybrid;

- d) a neutralizing probe diluent for diluting the probe and neutralizing the treated target nucleic acid sequence;
- e) a solid phase to which an anti-hybrid antibody or an anti-hybrid antibody fragment has been immobilized, wherein the antibody is specific for a hybrid formed by hybridization of the probe and the target nucleic acid sequence;
 - f) means for eliminating/any non-hybridized probe; and,
- g) means for detecting the hybrid formed by hybridization of the probe and the target nucleic acid sequence.
- 19. The kit of claim 18 wherein the means for eliminating non-hybridized probe is an enzyme that digests non-hybridized probe.
- 20. The kit of claim 18 wherein the target nucleic acid is DNA selected from the group consisting of human papillomavirus DNA, hepatitis B virus DNA and *Chlamydia* DNA.
- 21. The kit of claim 18 wherein the probe is an RNA sequence complementary to target DNA.
 - 22. The kit of claim 18 wherein the digesting enzyme is RNAase.
- 23. The kit of claim 18 wherein the base is sodium hydroxide in a concentration of between 0.1 and 2M.
- 24. The kit of claim 18 wherein the digesting enzyme and detecting means are combined in a single reagent.
- 25. A buffer/for use in a hybridization assay comprising 2-[bis(2-Hydroxyethyl) amino] ethane sulfonic acid and sodium acetate wherein the pH of the buffer is between approximately 5 and 5.5.
- 26. The buffer of claim 25 further comprising an antimicrobial agent, a metal chelating agent, a detergent, and a hybridization accelerator.
- 27. The buffer of claim-25 further comprising a probe in a concentration between 1 and 500 ng/ml for hybridization to a target nucleic acid.



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